Utilization of the QuantiFERON-TB Gold Test in a 2-Step Process with the Tuberculin Skin Test to Evaluate Healthcare Workers for Latent Tuberculosis

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Running Title: QuantiFERON-TB Gold Test for Latent Tuberculosis

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Abstract

A cost analysis of combining a tuberculin skin test (TST) and the QuantiFERON-TB Gold test (QFT-GT) to detect latent tuberculosis in newly hired healthcare workers was performed. An approximate reduction in 50% of the cost for additional care was realized when a positive TST was subsequently screened using a QFT-GT.

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Tuberculosis (TB) is a leading cause of morbidity and mortality worldwide with 9 million new cases and 2 million deaths reported in 2006 (13, 16). In the United States, 10 to 15 million people are estimated to have latent tuberculosis (LTB), an infection that is asymptomatic and non-infectious (13). The identification and appropriate treatment of people with LTB is necessary to control TB since some of these individuals will develop into active TB if not properly managed (13).

The tuberculin skin test (TST) was until recently the only available method used to detect LTB (1, 4, 5, 7, 10, 14). However, problems are associated with the TST such as a high false positive rate, interference by the Bacilli Calmette-Guérin (BCG) vaccination and a delayed result which requires two visits to the clinic, one for placement of the TST and another to evaluate the results of testing. This high false positive rate also leads to unnecessary procedures such as a chest x-ray (CXR), a more extensive systemic review, and isoniazid (INH) therapy (11, 14).

The QuantiFERON-TB Gold test (QFT-GT) (Cellestis Limited, Carnegie, Victoria, Australia) was recently approved by the FDA as a screening test to detect for active and LTB (8-11, 16). This assay tests whole blood and uses the enzyme-linked immunosorbent assay (ELISA) format to detect interferon gamma, a cytokine secreted by sensitized T-cell in response to specific Mycobacterium tuberculosis complex (MTBc) antigens which is absent from the BCG vaccine strain of M. bovis (8-11, 16). This study was conducted to assess the cost of using a 2-step process of evaluating a positive TST with the QFT-GT in new healthcare employees as a means to eliminate unneeded follow-up and treatment.
A total of 242 participants presenting to Employee Heath during pre-employment screening between April 2006 and April 2008 were enrolled in this study. The age of participants ranged from 18 to 64 years old with 141 females and 101 males. Of the participants, 123 were foreign born in the third world countries to include Africa, the Middle East, South East Asia, Central and South America. New employees were asked to complete a questionnaire that included the presence of medical conditions such as human immunodeficiency virus infection, diabetes, chronic pulmonary diseases, and previous TB disease, as well as risk of exposure to TB (such as close contact to patients with active TB or lived/traveled in an area where TB was highly endemic), history of BCG vaccination, and previous TST results. In addition, these individuals with a previous positive TST were asked about isoniazid (INH) prophylaxis and whether prophylaxis was completed. During this initial screen, a TST was placed and blood was drawn for the QFT-GT. Individuals with a positive TST by history were also automatically screened with a chest x-ray (CXR). The TST was performed according to the guidelines of American Thoracic Society and the Centers for Disease Control and Prevention (15). A TST induration or redness of ≥ 10 mm at 48 to 72 hours after the tuberculin injection was considered positive. The QFT-GT was performed according to the manufacturer’s recommendations.

A positive TST was identified for 132 (54.5%) of the new employees with 46 of these also positive by the QFT-GT (Table 1). All other employees that screened positive by the skin test were negative by the QFT-GT while all of the individuals negative by the TST were also negative by the QFT-GT. No changes consistent with tuberculosis were detected on the CXR for individuals with a positive TST. Discrepancies between the TST
and the QFT-GT were further evaluated by a comprehensive systematic review. No risk to having LTB was identified in the TST positive/QFT-GT negative individuals. All individuals with a positive QFT-GT were evaluated by a pulmonary specialist and offered INH where appropriate. These results showed that when compared with the QFT-GT, the sensitivity and specificity of the TST were 100% and 56%, respectively with positive predictive and negative predictive values of 34.8% and 100%.

New employees with a positive TST were given information on the pulmonary symptoms for TB and instructed to notify Employee Health if these symptoms were to occur. To assess for long-term outcomes, all TST positive employees were administered an annual screen to evaluate for pulmonary symptoms while TST negative individuals were given an annual TST as part of the routine policy for TB control. After a minimum of 18 months, no cases of TB have been identified in this group of patients. Soborg, et al also showed no tuberculous disease in TST positive/QFT-GT negative individuals after a follow-up period of 1.5 years (12).

These data demonstrated that the QFT-GT had higher specificity than the TST overall which agreed with other studies (2, 3, 5, 6, 11). Of interest was that of the 48 individuals who indicated prior BCG vaccination, 38 (82.6%) had a positive skin test and of these 13 (28.2%) were also QFT-GT positive. In this cohort of new employees tested, the high number of TST positive or QFT-GT positive individuals was expected since 50.8% (123/242) of the participants were foreign born from third world countries.

The estimated original screening costs of using the TST only was $726 ($3 for each participant) followed by TST with reflex of positive individuals to QFT-GT at $8,646±3960 ($3 for the TST and $60±30 for the QFT-GT on the 132 TST positive
individuals) and QFT-GT alone at $14,520 ± 7260 ($60 ± 30 for each participant). The evaluation and management of the TST positive individuals without using the QFT-GT was estimated to cost $86,460 based on a cost of $655 for each person ($70 for chest x-ray, $450 for health care provider fee [9 visits at $50 each], and $135 for laboratory fees [9 visits at $15 each]), while the management for the 46 individuals with positive QFT-GT results were calculated to be $30,130 ($655 for each). Overall costs for performing the TST only (TST placement and follow-up evaluation of the TST positive patients) was $87,186 followed by QFT-GT only at $44,650 ± 7260, and TST with reflex of TST positive patients to QFT-GT at $38,776 ± 3960. Thus, this evaluation showed the 2-step process of testing using the QFT-GT to further evaluate positive TST patients showed a reduction in cost of 55.5% when compared to TST testing only. Additional savings not included would be the cost for INH, the patient cost for lost work and travel for clinic visits, and the risk/side effects associated with INH therapy. Other studies have also shown a decrease in the number of candidates requiring INH treatment when the QFT-GT is included in the TB management program (3, 4, 7).

Initial screen with the QFT-GT alone also showed a substantial decrease in cost (48.8%) when compared to TST only testing. However, this reduction in cost was not as dramatic as the 2-step process even in a population where more than 50% of the individuals were TST positive. Methods to reduce the cost of the QFT-GT (such as larger volume testing) will make this screening scenario more attractive, especially in situations where a high TST positivity rate is noted and also in cases where a follow up testing and evaluation of TST results is not as accessible.
These data showed that a substantial savings could be realized by evaluating employees using a 2-step process to detect for LTB where a positive TST is confirmed by the QFT-GT. A long-term assessment for those employees who had a positive TST and a negative QFT-GT result is currently ongoing to monitor for the potential to develop TB.

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References


Table 1. Results from screening new employees with the TST and QFT-GT.

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<th>TST</th>
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Abbreviations: TST, tuberculin skin test; QFT-GT, QuantiFERON Gold test